

Genome wide profiling of dopaminergic neurons derived from human embryonic and induced pluripotent stem cells.

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Authors: Olga Momcilovic, Qiuyue Liu, Andrzej Swistowski, Tatiane Russo-Tait, Yiqiang Zhao, Mahendra S Rao, Xianmin Zeng

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Public Summary:

Recent advances in human embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) biology enable generation of dopaminergic neurons for potential therapy and drug screening. However, our current understanding of molecular and cellular signaling that controls human dopaminergic development and function is limited. Here, we report on a whole genome analysis of gene expression during dopaminergic differentiation of human ESC/iPSC using Illumina bead microarrays. We generated a transcriptome data set containing the expression levels of 28,688 unique transcripts by profiling five lines (three ESC and two iPSC lines) at four stages of differentiation: (1) undifferentiated ESC/iPSC, (2) neural stem cells, (3) dopaminergic precursors, and (4) dopaminergic neurons. This data set provides comprehensive information about genes expressed at each stage of differentiation. Our data indicate that distinct pathways are activated during neural and dopaminergic neuronal differentiation. For example, WNT, sonic hedgehog (SHH), and cAMP signaling pathways were found over-represented in dopaminergic populations by gene enrichment and pathway analysis, and their role was confirmed by perturbation analyses using RNAi (small interfering RNA of SHH and WNT) or small molecule [dibutyryl cyclic AMP (dcAMP)]. In summary, whole genome profiling of dopaminergic differentiation enables systematic analysis of genes/pathways, networks, and cellular/molecular processes that control cell fate decisions. Such analyses will serve as the foundation for better understanding of dopaminergic development, function, and development of future stem cell-based therapies.

Scientific Abstract:

Recent advances in human embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) biology enable generation of dopaminergic neurons for potential therapy and drug screening. However, our current understanding of molecular and cellular signaling that controls human dopaminergic development and function is limited. Here, we report on a whole genome analysis of gene expression during dopaminergic differentiation of human ESC/iPSC using Illumina bead microarrays. We generated a transcriptome data set containing the expression levels of 28,688 unique transcripts by profiling five lines (three ESC and two iPSC lines) at four stages of differentiation: (1) undifferentiated ESC/iPSC, (2) neural stem cells, (3) dopaminergic precursors, and (4) dopaminergic neurons. This data set provides comprehensive information about genes expressed at each stage of differentiation. Our data indicate that distinct pathways are activated during neural and dopaminergic neuronal differentiation. For example, WNT, sonic hedgehog (SHH), and cAMP signaling pathways were found over-represented in dopaminergic populations by gene enrichment and pathway analysis, and their role was confirmed by perturbation analyses using RNAi (small interfering RNA of SHH and WNT) or small molecule [dibutyryl cyclic AMP (dcAMP)]. In summary, whole genome profiling of dopaminergic differentiation enables systematic analysis of genes/pathways, networks, and cellular/molecular processes that control cell fate decisions. Such analyses will serve as the foundation for better understanding of dopaminergic development, function, and development of future stem cell-based therapies.

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